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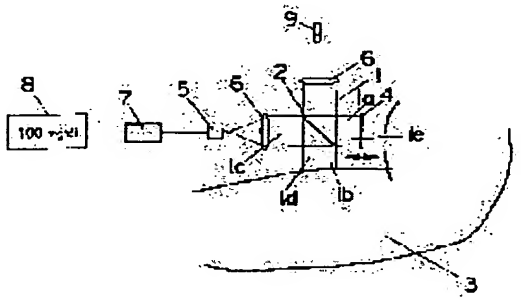
(54) MEASURING DEVICE FOR PROPERTIES OF ORGANISM TISSUE

(57)Abstract:
PROBLEM TO BE SOLVED: To provide a measuring device which can make accurate quantitative or qualitative analysis of the properties of organism tissue by making more district the signals related to the concentration change and physical property change of the component and the tissue.
SOLUTION: A measuring device for the properties of a organism tissue, which measures organism tissue properties in a organism 3 non-invasively, is composed of a beam splitter 2 to divide into two beams the near infrared rays 1 which are coherent or similar to it, a reflection mirror 4 to reflect one of the split beams 1a of the infrared rays so that it 1a interferes with the other beams 1b which has been reflected by the vital organism structure, a sensor 5 to sense the signal according to the reflective beam 1c having undergone an interference, and an information processing means 7 to make computational processing of the signal sensed by the sensor 5. It is arranged so that the position of the reflection mirror 4 relative to the reflective beam 1d reflected by the organism tissue can be set any as desired.



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JAPANESE [JP,10-000190,A]

CLAIMS DETAILED DESCRIPTION TECHNICAL FIELD PRIOR ART EFFECT OF THE INVENTION TECHNICAL PROBLEM MEANS DESCRIPTION OF DRAWINGS DRAWINGS

[Translation done.]

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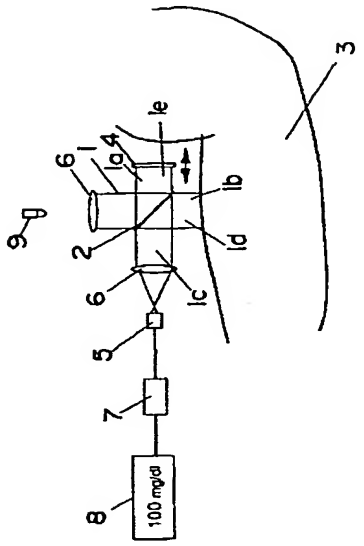
CLAIMS

[Claim(s)]
[Claim 1] the body tissue in a living body -- the body tissue which measures description non-invasive -- description -- with the beam splitter which is a measuring device and divides a coherent or near-infrared light near it into two The reflecting mirror reflected so that one light may be made to interfere among the divided near-infrared light with the light of another side reflected by the body tissue, the body tissue characterized by forming the location of the reflecting mirror to the reflected light which was equipped with the detector which detects the signal of the reflected light made to interfere, and the information processing means which carries out data processing of the signal detected with the detector, and was reflected by the body tissue, enabling a free setup, and changing -- description -- a measuring device.
[Claim 2] said body tissue -- the body tissue according to claim 1 characterized by description being the body fluid constituent concentration in the cell of a body tissue, or besides the cell of a body tissue -- description -- a measuring device.
[Claim 3] said body tissue -- the body tissue according to claim 1 or 2 characterized by using the coherent near-infrared light of at least one kind of wavelength which consists of a part of all fields that the body fluid constituent concentration which is description is glucose concentration, and were chosen from the field (at least 950-1150nm and 1250-1800nm) in the quantum of said glucose concentration, or fields -- description -- a measuring device.
[Claim 4] the body tissue according to claim 1 to 3 characterized by setting up the location of said reflecting mirror and changing so that the reflected light reflected in the reflected light reflected by the body tissue between 0.1-10.0mm hypodermically with the reflecting mirror may be made to interfere -- description -- a measuring device.
[Claim 5] the body tissue according to claim 1 to 4 which said body tissue is the body surface close-attendants side of arterial blood tubing near the body surface, or venous blood tubing, and is characterized by setting up the location of said reflecting mirror and changing so that the reflected light reflected in the reflected light reflected by this body tissue with the reflecting mirror may be made to interfere -- description -- a measuring device.
[Claim 6] the organization of a desired body tissue -- the body tissue according to claim 1 to 5 characterized by setting the location of said reflecting mirror as measuring description, and growing into it based on measurement of the size of the absorption of light of the petrographic constituent which is not desirable -- description -- a measuring device.
[Claim 7] the body tissue according to claim 6 characterized by detecting the size of the above-mentioned coherent near-infrared absorption of light in fat tissue by moving a reflecting mirror while using the coherent near-infrared light which said petrographic constituent which is not desirable is fat tissue, and becomes from a part of all field of one [at least] wavelength field (900-950nm and 1350-1420nm), or field -- description -- a measuring device.
[Claim 8] said body tissue -- the body tissue according to claim 1 characterized by descriptions being physical properties, such as hardness of a body tissue, and a consistency, -- description -- a measuring device.

[Translation done.]

Drawing selection Representative drawing



1 近赤外光
1a 光
1b 光
1c 干渉された反射光
1d 反射光
1e 反射光
2 ビームスプリッタ
3 生体
4 反射鏡
5 検出器
7 情報処理手段

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DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention] the body tissue to which this invention measures concentration, such as a glucose in blood, cholesterol, neutral fat, and a protein component, non-invasive especially using a near-infrared method about the measuring machine machine which measures the concentration of the indicator ingradient in body fluid, such as blood and cell sap, by non-invasion for the therapy of the health care or the illness -- description -- the body tissue which measures change of the body tissue represented by a measuring device or stiffness in shoulder and a breast cancer, liver cirrhosis, a fatty liver, and arteriosclerosis -- description -- it is related with a measuring device.
[0002]
[Description of the Prior Art] The measuring method of the glucose concentration in blood (blood sugar level) is explained about measurement of the conventional body fluid constituent concentration. The blood sugar meter used widely now is called the so-called biosensor which is made to carry out the chemical reaction of the glucose in the blood which collected blood, and measures glucose concentration. The fundamental biosensor consists of a part which identifies a measuring object component alternatively, and a part which changes into an electrical signal change which produces this measuring object component in the matter discernment by the part identified alternatively. The device with various electrochemistry measurement device, thermistor, field effect transistor (FET), photo transistor, etc. is used for the part changed into said electrical signal.
[0003] Moreover, the biological substances used for a matter discernment part (part which identifies said measuring object component alternatively) are cells (cell), such as an enzyme (enzyme), an antibody (antibody), binding protein (binding protein), lectin (lectin), an intracellular organelle (organelle), and a microorganism, an organization (tissue), etc., and these biological substances have the function to identify the specific matter. A biosensor is classified into an enzyme sensor, a microbial sensor, an immune sensor, an organelle sensor, and an organization sensor according to the biological substance to be used.
[0004] the enzyme which will be used for glucose detection if the glucose sensor by the enzyme electrode (matter discernment part using the enzyme as a biological substance) is taken for an example as an example of a blood sugar meter -- glucose oxidase (GOD) it is . This enzyme (GOD) The thing of the format which carries out the quantum of the glucose concentration because oxygen is consumed and the glucose sensor fixed in the poly membrane etc. catches change of this oxygen when the glucose in measurement liquid contacts the GOD fixed film is developed. A such blood collecting-type blood sugar meter is marketed widely, and is used for management of a diabetic's blood sugar level.
[0005] Moreover, the detection approach of a glucose as shown in JP,60-236631,A or JP,5-58735,B is one of things of the non-invasion which does not need blood collecting. The near-infrared light irradiated by the living body part is divided into a reference signal and a measurement signal, and the technique of measuring the blood sugar level is indicated by carrying out data processing of these values by these official reports. a source of the white light like [as the light source of near-infrared light] a tungsten halogen lamp in the above-mentioned technique -- a spectrum like an interference filter -- the approach and semi-conductor light emitting device (LED) which carry out a spectrum to wavelength predetermined

with a means are used. Moreover, as a detector of the near-infrared light which penetrated the living body part, the photodiode or a photo detector like a photo transistor is used. However, at present, these techniques have not reached practical use level.

[0006] The spectral analysis of the body fluid component by the above near-infrared light is the technique of attracting attention in recent years, and by the spectral analysis in a near infrared region as compared with the spectral analysis in an inside infrared region Since the water absorption spectrum is small, analysis of a water-solution system is possible, While it has the advantage in which the capacity which penetrates a living body is high, the signal level which belongs to molecular vibration has about 1/100, a small thing, and the demerit in which it is hard to specify attribution of a signal, as compared with an inside red field.

[0007] That is, when detecting the signal (signal) of the component (body fluid component) made into the purpose in a near infrared region, it has that the signal corresponding to concentration change of a component (body fluid component) made into the purpose is very small, and the problem that attribution of the signal is not clear in many cases. In order to solve such a problem, the so-called chemometrics technique combined with the statistical analysis technique or the multivariate-analysis technique (MLR), for example, a linearity multiple regression analysis, principal component regression analysis, and PLS regression analysis (partial least squares regressin) is used. However, although it is the technique excellent in such statistical analysis technique catching a minute signal change, and performing exact measuring (calibration), magnitude (SN ratio) of the signal (signal) of the target component (body fluid component) is not improved.

[0008] Then, a difference with the signal related to [for an improvement of an SN ratio / in / at the former / a near infrared region] concentration change of the component (body fluid component) of a reference signal and the purpose, Or the technique of having ****ed the noise component small enough and carrying out it is used by taking those ratios by clarifying concentration change (fluctuation) of the target component (body fluid component), or equalizing the signal (signal related to concentration change of the target component (body fluid component)) which carried out multiple-times measurement. Especially the above-mentioned equalization technique is used for various measurement from removal of a noise component being simply possible by making [many] the count of an average (count of measurement of a signal).

[0009] Moreover, by the conventional approach of making only carry out incidence of the light to a body tissue, and measuring the transmitted light or reflected light, it will be measured as a signal in the form which the transmitted lights or the reflected lights from an organization other than a body tissue to consider quantification of description as an intention superimposed, and has become the cause by which a noise component becomes large. then, description -- in measurement, the establishment and equipment of technique which can perform spectrum measurement (spectral-analysis measurement) of the form where the target organization is aimed at and moved are desired so that only the transmitted light or the reflected light from a body tissue to consider quantification of description as an intention may be obtained.

[0010]

[Problem(s) to be Solved by the Invention] therefore, the body tissue of non-invasion without the need of carrying out invasion of blood or the cell sap, and taking it out with a hypodermic needle etc. in case this invention measures the concentration of a living body's body fluid component -- description -- a measuring device -- It is a thing aiming at offering a measuring device. or physical properties, such as hardness of an organization in the living body, and a consistency, -- non-invasion and the body tissue measured in non-contact -- description -- in detail a near-infrared spectral-analysis method -- a body tissue -- description -- the reflected light of a from the organization aiming at analysis, or near the organization by detecting alternatively, when it is adapted for measurement and performs the quantum or qualitative analysis of a component of the purpose under organization the signal relevant to concentration change and physical-properties change of a component and an organization -- more -- clear -- carrying out -- an exact body tissue -- the body tissue which can perform the quantitative analysis or qualitative analysis of description -- description -- it aims at offering a measuring device.

[0011]

[Means for Solving the Problem] the body tissue of this invention according to claim 1 --

description -- a measuring device the body tissue in a living body 3 -- the body tissue which measures description non-invasive -- description -- with the beam splitter 2 which is a measuring device and divides the coherent or near-infrared light 1 near it into two The reflecting mirror 4 reflected so that one optical 1a may be made to interfere among the divided near-infrared light with optical 1b of another side reflected by the body tissue, It has the detector 5 which detects the signal of reflected light 1c made to interfere, and the information processing means 7 which carries out data processing of the signal detected with the detector 5, and is characterized by forming the location of the reflecting mirror 4 to 1d of reflected lights reflected by the body tissue, enabling a free setup, and changing.

[0012] moreover, the body tissue of this invention according to claim 2 -- description -- a measuring device -- the configuration of claim 1 -- in addition, said body tissue -- it is characterized by description being the body fluid constituent concentration in the cell of a body tissue, or besides the cell of a body tissue. moreover, the body tissue of this invention according to claim 3 -- description -- a measuring device -- claim 1 or the configuration of 2 -- in addition, said body tissue -- the body fluid constituent concentration which is description is glucose concentration, and it is characterized by using the coherent near-infrared light of at least one kind of wavelength which consists of a part of all fields chosen from the field (at least 950-1150nm and 1250-1800nm) in the quantum of said glucose concentration, or fields.

[0013] moreover, the body tissue of this invention according to claim 4 -- description -- a measuring device -- the configuration of claim 1 thru/or either of 3 -- in addition, it is characterized by setting up the location of said reflecting mirror 4 and changing so that reflected light 1e reflected in 1d of reflected lights reflected by the body tissue between 0.1-10.0mm hypodermically with the reflecting mirror 4 may be made to interfere. moreover, the body tissue of this invention according to claim 5 -- description -- a measuring device -- the configuration of claim 1 thru/or either of 4 -- in addition, said body tissue is the body surface close-attendants side of arterial blood tubing near the body surface, or venous blood tubing, and it is characterized by setting up the location of said reflecting mirror 4 and changing so that reflected light 1e reflected in 1d of reflected lights reflected by this body tissue with said reflecting mirror 4 may be made to interfere.

[0014] moreover, the body tissue of this invention according to claim 6 -- description -- a measuring device -- the configuration of claim 1 thru/or either of 5 -- in addition, the organization of a desired body tissue -- it is characterized by setting the location of a reflecting mirror 4 as measuring description, and growing into it based on measurement of the size of the absorption of light of the petrographic constituent which is not desirable. moreover, the body tissue of this invention according to claim 7 -- description -- a measuring device In addition to a configuration according to claim 6, said petrographic constituent which is not desirable is fat tissue. While using the coherent near-infrared light 1 which consists of a part of all field of one [at least] wavelength field (900-950nm and 1350-1420nm), or field It is characterized by detecting the size of absorption of said coherent near-infrared light 1 in fat tissue by moving a reflecting mirror 4.

[0015] moreover, the body tissue of this invention according to claim 8 -- description -- a measuring device -- the configuration of claim 1 -- in addition, said body tissue -- it is characterized by descriptions being physical properties, such as hardness of a body tissue, and a consistency.

[0016]

[Embodiment of the Invention] Hereafter, the gestalt of operation of this invention is explained. the body tissue shown in drawing 1 -- description -- if the coherent or near-infrared light 1 near it can be obtained on the wavelength of 750-2500nm as the light source 9 used in a measuring device, either can be used, for example, what processed the light of the laser light source, the thing which processed the light of a halogen lamp using the diffraction grating, the interferometer, the filter, etc., the LED light source, or the LED light source using the diffraction grating, the interferometer, the filter, etc. can be used.

[0017] As a beam splitter 2, if the above-mentioned near-infrared light 1, such as a half mirror, can be divided into two, either can be used and this beam splitter 2 is arranged between the above-mentioned light source 9 and a living body 3. As a reflecting mirror 4, one optical 1a of the light divided into two by the above-mentioned beam splitter 2 is reflected, and it is arranged in the location which optical 1a of one of these is drawn, and reaches. Moreover, the reflecting

mirror 4 is formed free [migration] so that the location to 1d of reflected lights reflected by the body tissue in the living body 3 which mentions later may be changed and it can set up freely.

[0018] As a detector 5, be [what is necessary / just although it has a light-receiving property in a near infrared region (near-infrared light 1)], in the near infrared region whose wavelength is 600-1100nm, the detector made from InGaAs can use suitably especially in the near infrared region whose wavelength the detector made from Si is 700-1700nm. If the signal from reflected light 1c which is obtained with a detector 5, which is mentioned later and in which it interfered is inputted as a data-processing means 7 and data processing of this signal can be carried out, either can be used and microcomputer PYUTA etc. can be illustrated.

[0019] With the above-mentioned data-processing means 7, the shape of raw somatic, for example, glucose concentration etc., is computed by carrying out data processing of the signal from reflected light 1c which is obtained with a detector 5 and in which it interfered according to the calibration curve prepared beforehand. The statistical analysis technique or the multivariate-analysis technique (MLR), for example, a linearity multiple regression analysis, principal component regression analysis, PLS regression analysis (partial least squares regressin), and the neural network technique can be used for creation of a calibration curve (measuring type). Such statistical analysis technique is the technique excellent in catching a minute signal change and performing exact measuring (calibration).

[0020] next, top Norio body tissue -- description -- actuation of a measuring device is explained. The near-infrared light 1 first irradiated from the light source 9 is divided into optical 1a drawn in the direction of a reflecting mirror 4, and optical 1b drawn in the direction of a living body 3 by the beam splitter 2. Next, while being reflected with a reflecting mirror 4 and setting to reflected light 1e optical 1a drawn in the direction of a reflecting plate 4, it is reflected by the body tissue inside a living body 3, and optical 1b drawn in the direction of a living body 3 becomes 1d of reflected lights which are the scattered light. Next, 1d of reflected lights reflected by the body tissue and reflected light 1e reflected with the reflecting mirror 4 interfere, and this reflected light 1c in which it interfered is led to a detector 5. And by carrying out data processing of the signal acquired from reflected light 1c which was led to the detector 5 next, and in which it interfered as mentioned above with the information processing means 7, the quantum of the description of the body tissue of a request aiming at measurement can be carried out, and it can be measured.

[0021] Since the spectral-analysis approach using near-infrared light (near infrared region) with a wavelength of 750-2500nm currently performed from the former as mentioned above has a small signal (signal) relevant to the component generally made into the purpose and the attribution is not clear in many cases, quantitative analysis is carried out difficult. For this reason, at the former, in order to improve an SN ratio, the difference of a certain criteria signal and purpose signal (signal from the body tissue aiming at measurement) is taken, or it pretreats taking and standardizing that ratio etc., and the quantum of the component of the purpose of the target body tissue is performed by applying the multivariate-analysis technique.

[0022] moreover, the light from a certain light source which contains two or more wavelength by the conventional spectral-analysis approach -- an interference filter or a diffraction grating -- serial -- a spectrum -- carrying out -- the light by which the spectrum was carried out -- one by one -- a ratio -- a measurement object is irradiated and it is asking for the absorbance and transmittance in each wavelength range by detecting the intensity of light penetrated or reflected, respectively. however, this technique -- a body tissue -- when it applies to measurement of description, it is detected as a spectrum which all the information that belongs to the constituent of the complicated body tissue which light penetrates or reflects superimposed -- ******** -- getting it blocked -- it becomes the spectrum with which the signal which originates in addition to the body tissue of the request which considers measurement as an intention (purpose) (attribution) was also contained. Therefore, the noise component to the signal which belongs to the component of the body tissue of the target request will increase, and an SN ratio will fall.

[0023] however, this invention top Norio body tissue -- description -- in a measuring device Since 1d of reflected lights reflected by the body tissue and reflected light 1e reflected with the reflecting mirror 4 are made to interfere and it was made to lead to a detector 5 The reflected light reflected light 1e reflected with the reflecting mirror 4 among 1d of reflected lights

reflected by the body tissue and whose phase correspond can be strengthened, and it can lead to a detector 5. The noise component to the signal which belongs to the component of a body tissue which reflects the reflected light reflected light 1e reflected with the reflecting mirror 4 and whose phase correspond can be reduced, and an SN ratio can be raised.
[0024] The distance between the body tissue which reflects the reflected light reflected light 1e reflected with the reflecting mirror 4 and whose phase correspond, and reflected light 1e and the point in which 1d interferes mutually It is the distance and the match between a reflecting mirror 4, and said reflected light 1e and the point in which 1d interferes mutually. Therefore, it is detectable whether the reflected light reflected from the body tissue of the location of living body 3 throat is strengthened by interference by finding the distance between the points in which a reflecting mirror 4, said reflected light 1e, and 1d of reflected lights interfere.
[0025] Moreover, since the above-mentioned reflecting mirror 4 was formed free [migration] to 1d of reflected lights reflected by the body tissue, the location of the point in which reflected light 1e and 1d of reflected lights interfere, and a reflecting mirror 4 can be set up freely. Therefore, by moving a reflecting mirror 4 to the point in which above-mentioned reflected light 1e and 1d of reflected lights interfere The phase of the reflected light from the body tissue which exists in the location of the arbitration in a living body's 3 depth direction, and the phase of reflected light 1e reflected with a reflecting mirror 4 can be made in agreement. The reflected light from the body tissue of the request set as the object of measurement can be strengthened alternatively, the noise component to the signal which belongs to the component of a desired body tissue set as the object of measurement can be reduced, and an SN ratio can be raised.
[0026] the body tissue of this invention -- description -- a measuring device sets the quantum of the concentration of the body fluid component in a body tissue cell or besides a body tissue cell as one purpose. on the other hand, it is in the quantum of the concentration of this body fluid component among the near-infrared light 1 of the field (1250-1800nm) near the first overtone of water, and the near-infrared light 1 of the field (800-1300nm) near the second harmonic overtone of water -- it is -- it carries out by using both. As a property of each field, in the field near the first overtone of water, while the spectrum signal which belongs to molecular vibration is large, the permeability of light is bad, and while the spectrum signal which belongs to molecular vibration in the field near the second harmonic overtone of water is small, it is rich in the permeability of light.
[0027] moreover, when the quantum of the concentration of the above-mentioned body fluid component is a quantum of glucose concentration The coherent near-infrared light of at least one kind of wavelength which consists of a part of all fields chosen from the wavelength field (950-1150nm and 1250-1800nm), or fields as a near-infrared light 1 irradiated from the light source 9, Especially, it is necessary to use wavelength (945**20nm, 965**20nm, 1015**30nm, 1100**30nm, 1400**20nm, 1450**20nm, 1500**20nm, and 1680**20nm) of coherent near-infrared light.
[0028] In the quantum of glucose concentration, as a signal of the field near the first overtone of water, that is, 950-1150nm, Preferably 945**20nm, 965**20nm, 1015**30nm, It is necessary to measure preferably 1250-1800nm 1100**30nm, using at least one wave of a signal (1400**20nm, 1450**20nm, 1500**20nm, and 1680**20nm) as a signal of the field near the second harmonic overtone of water.
[0029] Thus, precision can carry out preferably 950-1150nm of 1250-1800nm of glucose concentration quantitative analysis to the quantum of glucose concentration by using at least one wave of a signal (1400**20nm, 1450**20nm, 1500**20nm, and 1680**20nm) (near-infrared light 1) for 945**20nm, 965**20nm, 1015**30nm, and 1100**30nm preferably, and measuring.
[0030] The signal of each measured wavelength is changed into glucose concentration with the information processing means 7 using the calibration curve (measuring type) created beforehand, and is displayed as measured value with a display 8. Although creation of a calibration curve (measuring type) is usually created using some kinds of wavelength, if said wavelength is included in this invention, neither measurement wavelength nor a number will be restricted.
[0031] Moreover, in order to carry out the quantum of the glucose concentration in a body tissue cell or besides a body tissue cell as a substitution property of the blood sugar level The location of a reflecting mirror 4 can be set up so that it may be made to interfere in 1d (scattered light) of reflected lights from the body tissue made the purpose which is in the

location between 0.5-10.0mm preferably between 0.1-10.0mm hypodermically (object of measurement), and it is this. Precision can carry out glucose concentration as a substitution property of the blood sugar level quantitative analysis.
[0032] moreover, in performing a quantum for the quantum of concentration, especially glucose concentration of the body fluid component in a body tissue cell or besides a body tissue cell, reflected light 1e from a reflecting mirror 4 is made to interfere in 1d of reflected lights from the artery which flows near a living body's 3 body surface, or a vein, and it measures -- it is a very good approach. If the location of a reflecting mirror 4 is adjusted and set up in that case so that the reflected light in the body tissue of the side near [where optical 1b of another side divided by the beam splitter 2 of the near-infrared light 1 is irradiated] the near blood vessel (i.e., the body surface close attendants of a blood vessel) may interfere with reflected light 1e from a reflecting mirror 4, since the flowing blood has the property that dispersion is large and cannot use a blood vessel for measurement easily, a good spectrum (signal) will be obtained.
[0033] Moreover, it is necessary to measure by avoiding a subcutaneous adipose tissue in the quantum of glucose concentration from a viewpoint of obtaining a spectrum with a sufficient (high) SN ratio. Therefore, if it is very effective to move the location of a reflecting mirror 4 and to find the suitable setting location in measurement and it is in charge of detecting the location of the fat tissue, it carries out to the quantum of glucose concentration using the characteristic absorption of light of the fat tissue which is not desirable. In measuring size of the absorption of light in this fat tissue, it carries out using the coherent near-infrared light 1 which consists of a part of all field of a wavelength field (at least 900-950nm or 1350-1420nm), or field, and it compares whether it is that which this absorption calls at fat tissue, and judges.
[0034] the body tissue of this invention -- description -- another purpose of a measuring device -- a body tissue -- description is physical properties like the hardness of a body tissue, or a consistency, and is about these physical properties to carry out [qualitative analysis or] quantitative analysis. Physical properties like the hardness of a body tissue or a consistency are stiffness of the body specifically represented by stiffness in shoulder or change of the body tissue represented by a breast cancer, liver cirrhosis, a fatty liver, and arteriosclerosis.
[0035] such a body tissue -- the spectrum obtained from many test subjects is carried out to analysis of description using quantitative analysis or qualitative analysis. A linearity multiple regression analysis (MLR), principal component regression analysis, PLS regression analysis (partial least squares regressin), the neural network technique, and the neural network technique are used for quantitative analysis, and technique, such as discriminant analysis and a cluster analysis, can be used for qualitative analysis.
[0036] the body tissue which analyzes physical properties like the hardness of a body tissue, or a consistency (measurement) -- description -- a measuring device as well as the above can be formed. Although the decision of the measuring technique in the wavelength and the information-processing means 7 of the near-infrared light 1 irradiated from the light source 9 used for analysis performs by analyzing the spectrum (a signal) of much normal tissues and a lesion organization, as other decision technique of the measuring technique in the wavelength and the information-processing means 7 of the near-infrared light 1 irradiated from the light source 9 used for analysis, there is the approach of performing in invasion by an animal experiment etc. beforehand. This approach by irradiating the light which carried out the spectrum to the measured organization (both normal tissue and a lesion organization) which made it expose in invasion by technique, such as a diffraction grating and FT-IR, obtaining an absorption spectrum, and carrying out multivariate analysis of this absorption spectrum The measuring technique in the wavelength and the information processing means 7 of the near-infrared light 1 of using for a measuring device is determined. the body tissue of this invention -- description -- the measuring technique in this wavelength and information processing means 7 of the near-infrared light 1 that were determined -- using -- above -- the body tissue of this invention -- description -- the body tissue by the measuring device -- measurement of description (inch vivo measurement) It is made to carry out.
[0037] If an example is given, the cancer organization of a mouse which made it cancerate artificially will be exposed by cutting epidermal tissue open, and the spectrum of a cancer organization will be obtained by the above-mentioned technique. moreover, the thing which same actuation is carried out to the mouse of a large number containing a normal mouse, and a spectrum is obtained, and then is done for the qualitative analysis of these spectrums -- an

organization -- the wavelength distinction of description has a meaning -- taking up -- the body tissue of this invention -- description -- the wavelength of the near-infrared light 1 used for a measuring device is determined. and the near-infrared light 1 of this determined wavelength -- the body tissue of this invention -- description -- by analyzing description of the body tissue by the measuring device, the cancer onset can be distinguished by the body tissue. [0038] in addition, the body tissue of this invention -- description -- for raising the analysis precision of a measuring device -- further -- the body tissue of this invention -- description -- it is necessary to perform and carry out multivariate analysis of the analysis by the measuring device to many body tissues non-invasive

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TECHNICAL FIELD

[Field of the Invention] the body tissue to which this invention measures concentration, such as a glucose in blood, cholesterol, neutral fat, and a protein component, non-invasive especially using a near-infrared method about the measuring machine machine which measures the concentration of the indicator ingradient in body fluid, such as blood and cell sap, by non-invasion for the therapy of the health care or the illness -- description -- the body tissue which measures change of the body tissue represented by a measuring device or stiffness in shoulder and a breast cancer, liver cirrhosis, a fatty liver, and arteriosclerosis -- description -- it is related with a measuring device.

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PRIOR ART

[Description of the Prior Art] The measuring method of the glucose concentration in blood (blood sugar level) is explained about measurement of the conventional body fluid constituent concentration. The blood sugar meter used widely now is called the so-called biosensor which is made to carry out the chemical reaction of the glucose in the blood which collected blood, and measures glucose concentration. The fundamental biosensor consists of a part which identifies a measuring object component alternatively, and a part which changes into an electrical signal change which produces this measuring object component in the matter discernment by the part identified alternatively. The device with various electrochemistry measurement device, thermistor, field effect transistor (FET), photo transistor, etc. is used for the part changed into said electrical signal.
[0003] Moreover, the biological substances used for a matter discernment part (part which identifies said measuring object component alternatively) are cells (cell), such as an enzyme (enzyme), an antibody (antibody), binding protein (binding protein), lectin (lectin), an intracellular organelle (organelle), and a microorganism, an organization (tissue), etc., and these biological substances have the function to identify the specific matter. A biosensor is classified into an enzyme sensor, a microbial sensor, an immune sensor, an organelle sensor, and an organization sensor according to the biological substance to be used.
[0004] the enzyme which will be used for glucose detection if the glucose sensor by the enzyme electrode (matter discernment part using the enzyme as a biological substance) is taken for an example as an example of a blood sugar meter -- glucose oxidase (GOD) it is . This enzyme (GOD) The thing of the format which carries out the quantum of the glucose concentration because oxygen is consumed and the glucose sensor fixed in the poly membrane etc. catches change of this oxygen when the glucose in measurement liquid contacts the GOD fixed film is developed. A such blood collecting-type blood sugar meter is marketed widely, and is used for management of a diabetic's blood sugar level.
[0005] Moreover, the detection approach of a glucose as shown in JP,60-236631,A or JP,5-58735,B is one of things of the non-invasion which does not need blood collecting. The near-infrared light irradiated by the living body part is divided into a reference signal and a measurement signal, and the technique of measuring the blood sugar level is indicated by carrying out data processing of these values by these official reports. a source of the white light like [as the light source of near-infrared light] a tungsten halogen lamp in the above-mentioned technique -- a spectrum like an interference filter -- the approach and semi-conductor light emitting device (LED) which carry out a spectrum to wavelength predetermined with a means are used. Moreover, as a detector of the near-infrared light which penetrated the living body part, the photodiode or a photo detector like a photo transistor is used. However, at present, these techniques have not reached practical use level.
[0006] The spectral analysis of the body fluid component by the above near-infrared light is the technique of attracting attention in recent years, and by the spectral analysis in a near infrared region as compared with the spectral analysis in an inside infrared region Since the water absorption spectrum is small, analysis of a water-solution system is possible, While it has the advantage in which the capacity which penetrates a living body is high, the signal level which belongs to molecular vibration has about 1/100, a small thing, and the demerit in which it is hard to specify attribution of a signal, as compared with an inside red field.
[0007] That is, when detecting the signal (signal) of the component (body fluid component)

made into the purpose in a near infrared region, it has that the signal corresponding to concentration change of a component (body fluid component) made into the purpose is very small, and the problem that attribution of the signal is not clear in many cases. In order to solve such a problem, the so-called chemometrics technique combined with the statistical analysis technique or the multivariate-analysis technique (MLR), for example, a linearity multiple regression analysis, principal component regression analysis, and PLS regression analysis (partial least squares regressin) is used. However, although it is the technique excellent in such statistical analysis technique catching a minute signal change, and performing exact measuring (calibration), magnitude (SN ratio) of the signal (signal) of the target component (body fluid component) is not improved.

[0008] Then, a difference with the signal related to [for an improvement of an SN ratio / in / at the former / a near infrared region] concentration change of the component (body fluid component) of a reference signal and the purpose, Or the technique of having ****ed the noise component small enough and carrying out it is used by taking those ratios by clarifying concentration change (fluctuation) of the target component (body fluid component), or equalizing the signal (signal related to concentration change of the target component (body fluid component)) which carried out multiple-times measurement. Especially the above-mentioned equalization technique is used for various measurement from removal of a noise component being simply possible by making [many] the count of an average (count of measurement of a signal).

[0009] Moreover, by the conventional approach of making only carry out incidence of the light to a body tissue, and measuring the transmitted light or reflected light, it will be measured as a signal in the form which the transmitted lights or the reflected lights from an organization other than a body tissue to consider quantification of description as an intention superimposed, and has become the cause by which a noise component becomes large. then, description -- in measurement, the establishment and equipment of technique which can perform spectrum measurement (spectral-analysis measurement) of the form where the target organization is aimed at and moved are desired so that only the transmitted light or the reflected light from a body tissue to consider quantification of description as an intention may be obtained.

[Translation done.]

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EFFECT OF THE INVENTION

[Effect of the Invention] As mentioned above invention of this invention according to claim 1 The beam splitter which divides a coherent or near-infrared light near it into two, The reflecting mirror reflected so that one light may be made to interfere among the divided near-infrared light with the light of another side reflected by the body tissue, Since the location of the reflecting mirror to the reflected light which was equipped with the detector which detects the signal of the reflected light made to interfere, and the information processing means which carries out data processing of the signal detected with the detector, and was reflected by the body tissue was formed enabling a free setup By reflecting with a reflecting mirror so that one light may be made to interfere among the divided near-infrared light with the light of another side reflected by the body tissue The reflected light reflected by the body tissue of the phase of the reflected light reflected with the reflecting mirror and a phase in agreement can be strengthened alternatively. the description of the body tissue which reflects the reflected light of the phase of the reflected light reflected with the reflecting mirror, and a phase in agreement -- analysis can be analyzed with a sufficient precision by non-invasion -- that is, the signal relevant to concentration change and physical-properties change of the component of a body tissue and an organization -- more -- clear -- carrying out -- an exact body tissue -- the quantitative analysis or qualitative analysis of description can be performed.
[0059] And by forming the location of the reflecting mirror to the reflected light reflected by the body tissue, enabling a free setup, the phase of the reflected light from the body tissue of the location a living body's arbitration and the phase of the reflected light reflected with the reflecting mirror can be made in agreement, and the reflected light of a from near [of a location] a living body's arbitration the organization aiming at analysis or near the organization can be detected alternatively.
[0060] moreover, invention of this invention according to claim 2 -- said body tissue -- since description is the body fluid constituent concentration in the cell of a body tissue, or besides the cell of a body tissue, the body fluid constituent concentration in the cell of a body tissue or besides the cell of a body tissue can be analyzed with a sufficient precision by non-invasion. moreover, invention of this invention according to claim 3 -- said body tissue -- since the coherent near-infrared light of at least one kind of wavelength which consists of a part of all fields that the body fluid constituent concentration which is description is glucose concentration, and were chosen from the field (at least 950-1150nm and 1250-1800nm) in the quantum of said glucose concentration, or fields was used, glucose concentration can be analyzed with a sufficient precision by non-invasion.
[0061] Moreover, in measuring the glucose concentration of a body tissue as a substitution property of the blood sugar level, since the location of said reflecting mirror was set up so that the reflected light reflected in the reflected light reflected by the body tissue between 0.1-10.0mm hypodermically with the reflecting mirror might be made to interfere, invention of this invention according to claim 4 can analyze glucose concentration with a sufficient precision by non-invasion.
[0062] Moreover, said body tissue of invention of this invention according to claim 5 is the body surface close-attendants side of arterial blood tubing near the body surface, or venous blood tubing. Since the location of said reflecting mirror was set up so that the reflected light reflected in the reflected light reflected by this body tissue with the reflecting mirror might be made to interfere By making in agreement the phase of the reflected light from the body

surface close-attendants side of arterial blood tubing near [small] the body surface of dispersion, or venous blood tubing, and the phase of the reflected light reflected with the reflecting mirror Rather than the case where the phase of the reflected light from the large blood of dispersion and the phase of the reflected light reflected with the reflecting mirror are made in agreement, the shape of raw somatic and glucose concentration can be analyzed with a sufficient precision by non-invasion.

[0063] moreover, invention of this invention according to claim 6 -- the organization of a desired body tissue, since the location of said reflecting mirror was set as measuring description based on measurement of the size of the absorption of light of the petrographic constituent which is not desirable the organization of a desired body tissue -- in agreement with measuring description in the phase of the reflected light from the petrographic constituent which is not desirable, and the phase of the reflected light reflected with the reflecting mirror -- not making -- making -- a living body -- description can be analyzed with a sufficient precision by non-invasion.

[0064] Moreover, since invention of this invention according to claim 7 detected the size of the above-mentioned coherent near-infrared absorption of light in fat tissue by moving a reflecting mirror while using the coherent near-infrared light which said petrographic constituent which is not desirable is fat tissue, and becomes from a part of all field of one [at least] wavelength field (900-950nm and 1350-1420nm), or field, it can analyze with a sufficient precision whether it is the reflected light from fat tissue.

[0065] moreover, invention of this invention according to claim 8 -- said body tissue -- since descriptions are physical properties, such as hardness of a body tissue, and a consistency, analysis of the above-mentioned physical properties can be analyzed with a sufficient precision by non-invasion among the descriptions of a body tissue.

[Translation done.]

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TECHNICAL PROBLEM

[Problem(s) to be Solved by the Invention] therefore, the body tissue of non-invasion without the need of carrying out invasion of blood or the cell sap, and taking it out with a hypodermic needle etc. in case this invention measures the concentration of a living body's body fluid component -- description -- a measuring device -- It is a thing aiming at offering a measuring device. or physical properties, such as hardness of an organization in the living body, and a consistency, -- non-invasion and the body tissue measured in non-contact -- description -- in detail a near-infrared spectral-analysis method -- a body tissue -- description -- the reflected light of a from the organization aiming at analysis, or near the organization by detecting alternatively, when it is adapted for measurement and performs the quantum or qualitative analysis of a component of the purpose under organization the signal relevant to concentration change and physical-properties change of a component and an organization -- more -- clear -- carrying out -- an exact body tissue -- the body tissue which can perform the quantitative analysis or qualitative analysis of description -- description -- it aims at offering a measuring device.

[Translation done.]

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MEANS

[Means for Solving the Problem] the body tissue of this invention according to claim 1 -- description -- a measuring device the body tissue in a living body 3 -- the body tissue which measures description non-invasive -- description -- with the beam splitter 2 which is a measuring device and divides the coherent or near-infrared light 1 near it into two The reflecting mirror 4 reflected so that one optical 1a may be made to interfere among the divided near-infrared light with optical 1b of another side reflected by the body tissue, It has the detector 5 which detects the signal of reflected light 1c made to interfere, and the information processing means 7 which carries out data processing of the signal detected with the detector 5, and is characterized by forming the location of the reflecting mirror 4 to 1d of reflected lights reflected by the body tissue, enabling a free setup, and changing.
[0012] moreover, the body tissue of this invention according to claim 2 -- description -- a measuring device -- the configuration of claim 1 -- in addition, said body tissue -- it is characterized by description being the body fluid constituent concentration in the cell of a body tissue, or besides the cell of a body tissue. moreover, the body tissue of this invention according to claim 3 -- description -- a measuring device -- claim 1 or the configuration of 2 -- in addition, said body tissue -- the body fluid constituent concentration which is description is glucose concentration, and it is characterized by using the coherent near-infrared light of at least one kind of wavelength which consists of a part of all fields chosen from the field (at least 950-1150nm and 1250-1800nm) in the quantum of said glucose concentration, or fields.
[0013] moreover, the body tissue of this invention according to claim 4 -- description -- a measuring device -- the configuration of claim 1 thru/or either of 3 -- in addition, it is characterized by setting up the location of said reflecting mirror 4 and changing so that reflected light 1e reflected in 1d of reflected lights reflected by the body tissue between 0.1-10.0mm hypodermically with the reflecting mirror 4 may be made to interfere. moreover, the body tissue of this invention according to claim 5 -- description -- a measuring device -- the configuration of claim 1 thru/or either of 4 -- in addition, said body tissue is the body surface close-attendants side of arterial blood tubing near the body surface, or venous blood tubing, and it is characterized by setting up the location of said reflecting mirror 4 and changing so that reflected light 1e reflected in 1d of reflected lights reflected by this body tissue with said reflecting mirror 4 may be made to interfere.
[0014] moreover, the body tissue of this invention according to claim 6 -- description -- a measuring device -- the configuration of claim 1 thru/or either of 5 -- in addition, the organization of a desired body tissue -- it is characterized by setting the location of a reflecting mirror 4 as measuring description, and growing into it based on measurement of the size of the absorption of light of the petrographic constituent which is not desirable. moreover, the body tissue of this invention according to claim 7 -- description -- a measuring device In addition to a configuration according to claim 6, said petrographic constituent which is not desirable is fat tissue. While using the coherent near-infrared light 1 which consists of a part of all field of one [at least] wavelength field (900-950nm and 1350-1420nm), or field It is characterized by detecting the size of absorption of said coherent near-infrared light 1 in fat tissue by moving a reflecting mirror 4.
[0015] moreover, the body tissue of this invention according to claim 8 -- description -- a measuring device -- the configuration of claim 1 -- in addition, said body tissue -- it is characterized by descriptions being physical properties, such as hardness of a body tissue, and

a consistency.
[0016]
[Embodiment of the Invention] Hereafter, the gestalt of operation of this invention is explained. the body tissue shown in drawing 1 -- description -- if the coherent or near-infrared light 1 near it can be obtained on the wavelength of 750-2500nm as the light source 9 used in a measuring device, either can be used, for example, what processed the light of the laser light source, the thing which processed the light of a halogen lamp using the diffraction grating, the interferometer, the filter, etc., the LED light source, or the LED light source using the diffraction grating, the interferometer, the filter, etc. can be used.
[0017] As a beam splitter 2, if the above-mentioned near-infrared light 1, such as a half mirror, can be divided into two, either can be used and this beam splitter 2 is arranged between the above-mentioned light source 9 and a living body 3. As a reflecting mirror 4, one optical 1a of the light divided into two by the above-mentioned beam splitter 2 is reflected, and it is arranged in the location which optical 1a of one of these is drawn, and reaches. Moreover, the reflecting mirror 4 is formed free [migration] so that the location to 1d of reflected lights reflected by the body tissue in the living body 3 which mentions later may be changed and it can set up freely.
[0018] As a detector 5, be [what is necessary / just although it has a light-receiving property in a near infrared region (near-infrared light 1)], in the near infrared region whose wavelength is 600-1100nm, the detector made from InGaAs can use suitably especially in the near infrared region whose wavelength the detector made from Si is 700-1700nm. If the signal from reflected light 1c which is obtained with a detector 5, which is mentioned later and in which it interfered is inputted as a data-processing means 7 and data processing of this signal can be carried out, either can be used and microcomputer PYUTA etc. can be illustrated.
[0019] With the above-mentioned data-processing means 7, the shape of raw somatic, for example, glucose concentration etc., is computed by carrying out data processing of the signal from reflected light 1c which is obtained with a detector 5 and in which it interfered according to the calibration curve prepared beforehand. The statistical analysis technique or the multivariate-analysis technique (MLR), for example, a linearity multiple regression analysis, principal component regression analysis, PLS regression analysis (partial least squares regressin), and the neural network technique can be used for creation of a calibration curve (measuring type). Such statistical analysis technique is the technique excellent in catching a minute signal change and performing exact measuring (calibration).
[0020] next, top Norio body tissue -- description -- actuation of a measuring device is explained. The near-infrared light 1 first irradiated from the light source 9 is divided into optical 1a drawn in the direction of a reflecting mirror 4, and optical 1b drawn in the direction of a living body 3 by the beam splitter 2. Next, while being reflected with a reflecting mirror 4 and setting to reflected light 1e optical 1a drawn in the direction of a reflecting plate 4, it is reflected by the body tissue inside a living body 3, and optical 1b drawn in the direction of a living body 3 becomes 1d of reflected lights which are the scattered light. Next, 1d of reflected lights reflected by the body tissue and reflected light 1e reflected with the reflecting mirror 4 interfere, and this reflected light 1c in which it interfered is led to a detector 5. And by carrying out data processing of the signal acquired from reflected light 1c which was led to the detector 5 next, and in which it interfered as mentioned above with the information processing means 7, the quantum of the description of the body tissue of a request aiming at measurement can be carried out, and it can be measured.
[0021] Since the spectral-analysis approach using near-infrared light (near infrared region) with a wavelength of 750-2500nm currently performed from the former as mentioned above has a small signal (signal) relevant to the component generally made into the purpose and the attribution is not clear in many cases, quantitative analysis is carried out difficult. For this reason, at the former, in order to improve an SN ratio, the difference of a certain criteria signal and purpose signal (signal from the body tissue aiming at measurement) is taken, or it pretreats taking and standardizing that ratio etc., and the quantum of the component of the purpose of the target body tissue is performed by applying the multivariate-analysis technique.
[0022] moreover, the light from a certain light source which contains two or more wavelength by the conventional spectral-analysis approach -- an interference filter or a diffraction grating -- serial -- a spectrum -- carrying out -- the light by which the spectrum was carried out -- one

by one -- a ratio -- a measurement object is irradiated and it is asking for the absorbance and transmittance in each wavelength range by detecting the intensity of light penetrated or reflected, respectively. however, this technique -- a body tissue -- when it applies to measurement of description, it is detected as a spectrum which all the information that belongs to the constituent of the complicated body tissue which light penetrates or reflects superimposed -- ******** -- getting it blocked -- it becomes the spectrum with which the signal which originates in addition to the body tissue of the request which considers measurement as an intention (purpose) (attribution) was also contained. Therefore, the noise component to the signal which belongs to the component of the body tissue of the target request will increase, and an SN ratio will fall.

[0023] however, this invention top Norio body tissue -- description -- in a measuring device Since 1d of reflected lights reflected by the body tissue and reflected light 1e reflected with the reflecting mirror 4 are made to interfere and it was made to lead to a detector 5 The reflected light reflected light 1e reflected with the reflecting mirror 4 among 1d of reflected lights reflected by the body tissue and whose phase correspond can be strengthened, and it can lead to a detector 5. The noise component to the signal which belongs to the component of a body tissue which reflects the reflected light reflected light 1e reflected with the reflecting mirror 4 and whose phase correspond can be reduced, and an SN ratio can be raised.

[0024] The distance between the body tissue which reflects the reflected light reflected light 1e reflected with the reflecting mirror 4 and whose phase correspond, and reflected light 1e and the point in which 1d interferes mutually It is the distance and the match between a reflecting mirror 4, and said reflected light 1e and the point in which 1d interferes mutually. Therefore, it is detectable whether the reflected light reflected from the body tissue of the location of living body 3 throat is strengthened by interference by finding the distance between the points in which a reflecting mirror 4, said reflected light 1e, and 1d of reflected lights interfere.

[0025] Moreover, since the above-mentioned reflecting mirror 4 was formed free [migration] to 1d of reflected lights reflected by the body tissue, the location of the point in which reflected light 1e and 1d of reflected lights interfere, and a reflecting mirror 4 can be set up freely. Therefore, by moving a reflecting mirror 4 to the point in which above-mentioned reflected light 1e and 1d of reflected lights interfere The phase of the reflected light from the body tissue which exists in the location of the arbitration in a living body's 3 depth direction, and the phase of reflected light 1e reflected with a reflecting mirror 4 can be made in agreement. The reflected light from the body tissue of the request set as the object of measurement can be strengthened alternatively, the noise component to the signal which belongs to the component of a desired body tissue set as the object of measurement can be reduced, and an SN ratio can be raised.

[0026] the body tissue of this invention -- description -- a measuring device sets the quantum of the concentration of the body fluid component in a body tissue cell or besides a body tissue cell as one purpose. on the other hand, it is in the quantum of the concentration of this body fluid component among the near-infrared light 1 of the field (1250-1800nm) near the first overtone of water, and the near-infrared light 1 of the field (800-1300nm) near the second harmonic overtone of water -- it is -- it carries out by using both. As a property of each field, in the field near the first overtone of water, while the spectrum signal which belongs to molecular vibration is large, the permeability of light is bad, and while the spectrum signal which belongs to molecular vibration in the field near the second harmonic overtone of water is small, it is rich in the permeability of light.

[0027] moreover, when the quantum of the concentration of the above-mentioned body fluid component is a quantum of glucose concentration The coherent near-infrared light of at least one kind of wavelength which consists of a part of all fields chosen from the wavelength field (950-1150nm and 1250-1800nm), or fields as a near-infrared light 1 irradiated from the light source 9, Especially, it is necessary to use wavelength (945**20nm, 965**20nm, 1015**30nm, 1100**30nm, 1400**20nm, 1450**20nm, 1500**20nm, and 1680**20nm) of coherent near-infrared light.

[0028] In the quantum of glucose concentration, as a signal of the field near the first overtone of water, that is, 950-1150nm, Preferably 945**20nm, 965**20nm, 1015**30nm, It is necessary to measure preferably 1250-1800nm 1100**30nm, using at least one wave of a signal (1400**20nm, 1450**20nm, 1500**20nm, and 1680**20nm) as a signal of the field near the second harmonic overtone of water.

[0029] Thus, precision can carry out preferably 950-1150nm of 1250-1800nm of glucose concentration quantitative analysis to the quantum of glucose concentration by using at least one wave of a signal (1400**20nm, 1450**20nm, 1500**20nm, and 1680**20nm) (near-infrared light 1) for 945**20nm, 965**20nm, 1015**30nm, and 1100**30nm preferably, and measuring.
[0030] The signal of each measured wavelength is changed into glucose concentration with the information processing means 7 using the calibration curve (measuring type) created beforehand, and is displayed as measured value with a display 8. Although creation of a calibration curve (measuring type) is usually created using some kinds of wavelength, if said wavelength is included in this invention, neither measurement wavelength nor a number will be restricted.
[0031] Moreover, in order to carry out the quantum of the glucose concentration in a body tissue cell or besides a body tissue cell as a substitution property of the blood sugar level The location of a reflecting mirror 4 can be set up so that it may be made to interfere in 1d (scattered light) of reflected lights from the body tissue made the purpose which is in the location between 0.5-10.0mm preferably between 0.1-10.0mm hypodermically (object of measurement), and it is this. Precision can carry out glucose concentration as a substitution property of the blood sugar level quantitative analysis.
[0032] moreover, in performing a quantum for the quantum of concentration, especially glucose concentration of the body fluid component in a body tissue cell or besides a body tissue cell, reflected light 1e from a reflecting mirror 4 is made to interfere in 1d of reflected lights from the artery which flows near a living body's 3 body surface, or a vein, and it measures -- it is a very good approach. If the location of a reflecting mirror 4 is adjusted and set up in that case so that the reflected light in the body tissue of the side near [where optical 1b of another side divided by the beam splitter 2 of the near-infrared light 1 is irradiated] the near blood vessel (i.e., the body surface close attendants of a blood vessel) may interfere with reflected light 1e from a reflecting mirror 4, since the flowing blood has the property that dispersion is large and cannot use a blood vessel for measurement easily, a good spectrum (signal) will be obtained.
[0033]

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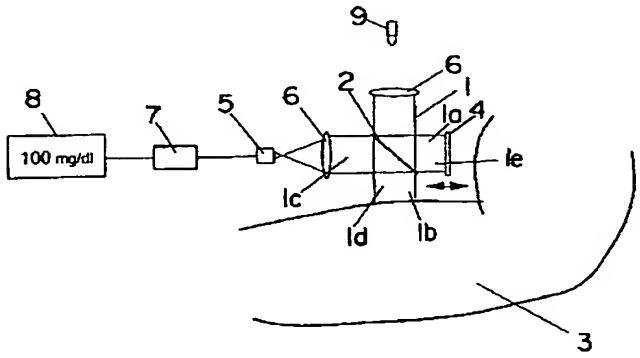
DESCRIPTION OF DRAWINGS

[Brief Description of the Drawings]
[Drawing 1] It is the schematic diagram showing the gestalt of 1 operation of this invention.
[Drawing 2] It is the schematic diagram showing the gestalt of other operations same as the above.
[Description of Notations]
1 Near-infrared Light
1a Light
1b Light
1c The reflected light in which it interfered
1d Reflected light
1e Reflected light
2 Beam Splitter
3 Living Body
4 Reflecting Mirror
5 Detector
7 Information Processing Means

[Translation done.]

Drawing selection drawing 1

1 近赤外光
1 a 光
1 b 光
1 c 干渉された反射光
1 d 反射光
1 e 反射光
2 ビームスプリッタ
3 生体
4 反射鏡
5 検出器
7 情報処理手段



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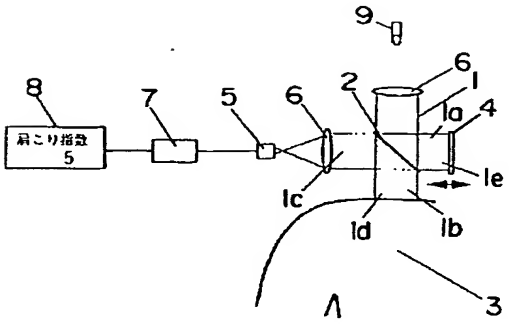
Drawing selection drawing 2



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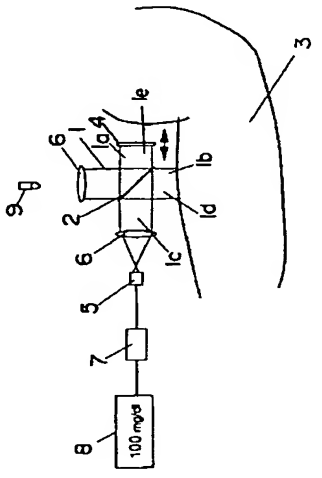
(54)【発明の名称】　生体組織性状測定装置

(57)【要約】

【課題】　成分や組織の濃度変化や物性変化に関連する信号をより明確にして正確な生体組織性状の定量分析あるいは定性分析をおこなうことができる生体組織性状測定装置を提供する。

【解決手段】　生体３中の生体組織性状を非侵襲的に計測する生体組織性状測定装置に関する。コヒーレントあるいはそれに近い近赤外光１を二つに分割するビームスプリッタ２。分割された近赤外光のうち一方の光１ａを生体組織で反射される他方の光１ｂと干渉させるように反射する反射鏡４。干渉させた反射光１ｃの信号を検出する検出器５。検出器５で検出された信号を演算処理する情報処理手段７とを備える。生体組織で反射された反射光１ｄに対する反射鏡４の位置を設定自在に形成する。



1 近赤外光
1a 光
1b 光
1c 干渉された反射光
1d 反射光
1e 反射光
2 ビームスプリッタ
3 生体
4 反射鏡
5 検出器
7 情報処理手段

【特許請求の範囲】
【請求項１】　生体中の生体組織性状を非侵襲的に計測する生体組織性状測定装置であって、コヒーレントあるいはそれに近い近赤外光を二つに分割するビームスプリッタと、分割された近赤外光のうち一方の光を生体組織で反射される他方の光と干渉させるように反射する反射鏡と、干渉させた反射光の信号を検出する検出器と、検出器で検出された信号を演算処理する情報処理手段とを備え、生体組織で反射された反射光に対する反射鏡の位置を設定自在に形成して成ることを特徴とする生体組織性状測定装置。
【請求項２】　前記生体組織性状が生体組織の細胞中あるいは生体組織の細胞外の体液成分濃度であることを特徴とする請求項１に記載の生体組織性状測定装置。
【請求項３】　前記生体組織性状である体液成分濃度がグルコース濃度であって、前記グルコース濃度の定量にあたって少なくとも９５０～１１５０ｎｍ及び１２５０～１８００ｎｍの領域から選択された全領域あるいは領域の一部からなる少なくとも一種類の波長のコヒーレント近赤外光を用いることを特徴とする請求項１又は２に記載の生体組織性状測定装置。
【請求項４】　皮下０．１～１０．０ｍｍの間の生体組織で反射された反射光に反射鏡で反射された反射光を干渉させるように前記反射鏡の位置を設定して成ることを特徴とする請求項１乃至３のいずれかに記載の生体組織性状測定装置。
【請求項５】　前記生体組織が体表面近傍の動脈血管あるいは静脈血管の体表側近傍であって、この生体組織で反射された反射光に反射鏡で反射された反射光を干渉させるように前記反射鏡の位置を設定して成ることを特徴とする請求項１乃至４のいずれかに記載の生体組織性状測定装置。
【請求項６】　所望の生体組織の組織性状を測定するのに好ましくない組織成分の光の吸収の大小の測定に基づいて、前記反射鏡の位置を設定して成ることを特徴とする請求項１乃至５のいずれかに記載の生体組織性状測定装置。
【請求項７】　前記好ましくない組織成分が脂肪組織であって、９００～９５０ｎｍ及び１３５０～１４２０ｎｍの少なくとも一方の波長領域の全領域あるいは領域の一部からなるコヒーレント近赤外光を用いると共に反射鏡を移動させることによって脂肪組織での上記コヒーレント近赤外光の吸収の大小を検出することを特徴とする請求項６に記載の生体組織性状測定装置。
【請求項８】　前記生体組織性状が生体組織の固さや密度等の物性であることを特徴とする請求項１に記載の生体組織性状測定装置。
【発明の詳細な説明】
【０００１】
【発明の属する技術分野】本発明は、健康管理や疾病の治療のために、血液や細胞液などの体液中の指標成分の濃度を非侵襲で測定する計測機器に関するものであり、特に近赤外法を用いて血液中のグルコース、コレステロール、中性脂肪、蛋白成分などの濃度を非侵襲的に測定する生体組織性状測定装置、あるいは肩こりや乳癌、肝硬変、脂肪肝、動脈硬化に代表される生体組織の変化を測定する生体組織性状測定装置に関するものである。
【０００２】
【従来の技術】従来の体液成分濃度の測定に関して、血液中のグルコース濃度（血糖値）の測定方法を説明する。現在広く用いられている血糖計は、採血した血液中のグルコースを化学反応させてグルコース濃度を測定する、いわゆるバイオセンサと呼ばれるものである。基本的なバイオセンサは、測定対象成分を選択的に識別する部位と、この測定対象成分を選択的に識別する部位による物質識別で生じる変化を電気信号に変換する部位から構成されている。前記電気信号に変換する部位には、電気化学計測デバイス、サーミスタ、電界効果形トランジスタ（ＦＥＴ）、ホトトランジスタなどの多様なデバイスが用いられている。
【０００３】また物質識別部位（前記測定対象成分を選択的に識別する部位）に用いられる生体物質は、酵素(enzyme)、抗体(antibody)、結合タンパク質(binding protein)、レクチン(lectin)、細胞内小器官(organelle)、微生物などの細胞(cell)、組織(tissue)などで、これらの生体物質は特定の物質を識別する機能を有している。バイオセンサは利用する生体物質によって、酵素センサ、微生物センサ、免疫センサ、オルガネラ・センサ、組織センサに分類される。
【０００４】血糖計の例として酵素電極（生体物質として酵素を用いた物質識別部位）によるグルコースセンサを例に採ると、グルコース検知に使われる酵素は、グルコースオキシダーゼ(GOD)である。この酵素(GOD)を高分子膜などに固定化したグルコースセンサは、測定液中のグルコースがＧＯＤ固定化膜に接触することによって酸素が消費され、この酸素の変化をとらえることでグルコース濃度を定量する形式のものが開発されている。このような採血式の血糖計は広く市販され、糖尿病患者の血糖値の管理に利用されている。
【０００５】また採血を必要としない非侵襲のものとしては、特開昭６０－２３６６３１号公報あるいは特公平５－５８７３５号公報に示されているようなグルコースの検出方法がある。これらの公報には、生体部位に照射された近赤外光を基準信号と測定信号とに分け、これらの値を演算処理することにより血糖値を測定する手法が開示されている。上記手法において近赤外光の光源としては、タングステン・ハロゲンランプのような白色光源を干渉フィルタのような分光手段で所定の波長に分光する方法や半導体発光素子（ＬＥＤ）が用いられている。また生体部位を透過した近赤外光の検出器としては、フ

ォトダイオードあるいはフォトトランジスタのような受光素子が用いられている。しかしながら、現時点ではこれらの技術が実用レベルに達していない。

【０００６】上記のような近赤外光による体液成分の分光分析は近年注目されている手法であり、中赤外領域における分光分析と比較して近赤外領域における分光分析では、水の吸収スペクトルが小さいので、水溶液系の分析が可能であることや、生体を透過する能力が高いという長所を有する反面、分子振動に帰属する信号レベルが中赤領域と比較して１００分の１程度と小さいことや、信号の帰属が特定しにくいという短所を有するものである。

【０００７】すなわち、近赤外領域において目的とする成分（体液成分）のシグナル（信号）を検知する場合、目的とする成分（体液成分）の濃度変化に対応する信号が非常に小さいこと、またその信号の帰属が明瞭でない場合が多いという問題を抱えている。このような問題を解決するために統計解析手法あるいは多変量解析手法、例えば線形重回帰分析（ＭＬＲ）、主成分回帰分析、ＰＬＳ回帰分析（partial least squares regressin ）と組み合わせるいわゆるケモメトリクス手法が用いられている。しかしこれらの統計的解析手法は微小な信号変化をとらえ、正確な検量（キャリブレーション）をおこなうのに優れた手法ではあるが、目的の成分（体液成分）のシグナル（信号）の大きさ（ＳＮ比）を改善するものではない。

【０００８】そこで従来では近赤外領域におけるＳＮ比の改善のために、基準信号と目的の成分（体液成分）の濃度変化に関係する信号との差、あるいはそれらの比をとることにより目的の成分（体液成分）の濃度変化（変動）を明確にしたり、複数回計測した信号（目的の成分（体液成分）の濃度変化に関係する信号）を平均化することによりノイズ成分を小さくしたりする手法が用いられている。特に上記平均化手法は、平均回数（信号の計測回数）を多くすることで簡単にノイズ成分の除去が可能であることから様々な測定に利用されている。

【０００９】また生体組織に単に光を入射させてその透過光あるいは反射光を測定する従来の方法では、性状の定量化を意図とする目的の生体組織以外の組織からの透過光あるいは反射光が重畳した形で信号として測定されることになってしまい、ノイズ成分が大きくなる原因となっている。そこで性状測定において、性状の定量化を意図とする目的の生体組織からの透過光あるいは反射光のみが得られるように、目的とする組織をねらい打つ形のスペクトル測定（分光分析測定）をおこなうことができるような手法の確立や装置が望まれている。

【００１０】

【発明が解決しようとする課題】従って本発明は、生体の体液成分の濃度を測定する際に、血液あるいは細胞液などを注射針などで侵襲して取り出す必要のない非侵襲の生体組織性状測定装置、あるいは生体内組織の固さや密度等の物性を非侵襲、非接触的に計測する生体組織性状測定装置を提供することを目的とするものであり、詳しくは、近赤外分光分析法を生体組織性状測定に適応して組織中の目的の成分の定量あるいは定性分析をおこなう場合において、分析を目的とする組織あるいは組織近傍からの反射光を選択的に検知することで、成分や組織の濃度変化や物性変化に関連する信号をより明確にして正確な生体組織性状の定量分析あるいは定性分析をおこなうことができる生体組織性状測定装置を提供することを目的とするものである。

【００１１】

【課題を解決するための手段】本発明の請求項１に記載の生体組織性状測定装置は、生体３中の生体組織性状を非侵襲的に計測する生体組織性状測定装置であって、コヒーレントあるいはそれに近い近赤外光１を二つに分割するビームスプリッタ２と、分割された近赤外光のうち一方の光１ａを生体組織で反射される他方の光１ｂと干渉させるように反射する反射鏡４と、干渉させた反射光１ｃの信号を検出する検出器５と、検出器５で検出された信号を演算処理する情報処理手段７とを備え、生体組織で反射された反射光１ｄに対する反射鏡４の位置を設定自在に形成して成ることを特徴とするものである。

【００１２】また本発明の請求項２に記載の生体組織性状測定装置は、請求項１の構成に加えて、前記生体組織性状が生体組織の細胞中あるいは生体組織の細胞外の体液成分濃度であることを特徴とするものである。また本発明の請求項３に記載の生体組織性状測定装置は、請求項１又は２の構成に加えて、前記生体組織性状である体液成分濃度がグルコース濃度であって、前記グルコース濃度の定量にあたって少なくとも９５０～１１５０ｎｍ及び１２５０～１８００ｎｍの領域から選択された全領域あるいは領域の一部からなる少なくとも一種類の波長のコヒーレント近赤外光を用いることを特徴とするものである。

【００１３】また本発明の請求項４に記載の生体組織性状測定装置は、請求項１乃至３のいずれかの構成に加えて、皮下０．１～１０．０ｍｍの間の生体組織で反射された反射光１ｄに反射鏡４で反射された反射光１ｅを干渉させるように前記反射鏡４の位置を設定して成ることを特徴とするものである。また本発明の請求項５に記載の生体組織性状測定装置は、請求項１乃至４のいずれかの構成に加えて、前記生体組織が体表面近傍の動脈血管あるいは静脈血管の体表側近傍であって、この生体組織で反射された反射光１ｄに前記反射鏡４で反射された反射光１ｅを干渉させるように前記反射鏡４の位置を設定して成ることを特徴とするものである。

【００１４】また本発明の請求項６に記載の生体組織性状測定装置は、請求項１乃至５のいずれかの構成に加えて、所望の生体組織の組織性状を測定するのに好ましく

ない組織成分の光の吸収の大小の測定に基づいて、反射鏡４の位置を設定して成ることを特徴とするものである。また本発明の請求項７に記載の生体組織性状測定装置は、請求項６に記載の構成に加えて、前記好ましくない組織成分が脂肪組織であって、９００～９５０ｎｍ及び１３５０～１４２０ｎｍの少なくとも一方の波長領域の全領域あるいは領域の一部からなるコヒーレント近赤外光１を用いると共に反射鏡４を移動させることによって脂肪組織での前記コヒーレント近赤外光１の吸収の大小を検出することを特徴とするものである。

【００１５】また本発明の請求項８に記載の生体組織性状測定装置は、請求項１の構成に加えて、前記生体組織性状が生体組織の固さや密度等の物性であることを特徴とするものである。

【００１６】

【発明の実施の形態】以下、本発明の実施の形態を説明する。図１に示す生体組織性状測定装置において使用する光源９としては、７５０～２５００ｎｍの波長でコヒーレントあるいはそれに近い近赤外光１を得られるものであれば何れでも用いることができ、例えばレーザー光源、ハロゲンランプの光を回折格子や干渉計やフィルター等を利用して処理したもの、ＬＥＤ光源あるいはＬＥＤ光源の光を回折格子や干渉計やフィルター等を利用して処理したものなどを用いることができる。

【００１７】ビームスプリッタ２としては、ハーフミラー等の上記近赤外光１を二つに分割することができるものであれば何れでも用いることができ、このビームスプリッタ２は上記光源９と生体３の間に配置されている。反射鏡４としては、上記ビームスプリッタ２で二つに分割された光のうちの一方の光１ａを反射するものであって、この一方の光１ａが導かれて到達する位置に配置されている。また反射鏡４は後述する生体３中の生体組織で反射された反射光１ｄに対する位置を変更して自由に設定することができるように移動自在に形成されている。

【００１８】検出器５としては、近赤外領域（近赤外光１）に受光特性を有するものであればよいが、波長が６００～１１００ｎｍの近赤外領域ではＳｉ製のディテクターが、波長が７００～１７００ｎｍの近赤外領域ではＩｎＧａＡｓ製のディテクターが特に好適に用いることができる。演算処理手段７としては、検出器５で得られる後述する干渉された反射光１ｃからの信号が入力されてこの信号を演算処理することができるものであれば何れでも使用することができ、マイクロコンピュタなどを例示することができる。

【００１９】上記演算処理手段７では、検出器５で得られる干渉された反射光１ｃからの信号を予め用意された検量線にしたがって演算処理して生体性状、例えばグルコース濃度などを算出するものである。検量線（検量式）の作成には、統計的解析手法あるいは多変量解析手法、例えば線形重回帰分析（ＭＬＲ）、主成分回帰分析、ＰＬＳ回帰分析（partial least squares regression）、ニューラルネット手法を用いることができる。これらの統計的解析手法は微小な信号変化をとらえ、正確な検量（キャリブレーション）をおこなうのに優れた手法である。

【００２０】次に上記生体組織性状測定装置の動作について説明する。先ず光源９から照射された近赤外光１はビームスプリッタ２によって、反射鏡４の方向に導かれる光１ａと、生体３の方向に導かれる光１ｂとに分割される。次に反射板４の方向に導かれた光１ａは反射鏡４で反射されて反射光１ｅとなると共に生体３の方向に導かれた光１ｂは生体３の内部の生体組織で反射されて散乱光である反射光１ｄとなる。次に生体組織で反射された反射光１ｄと反射鏡４で反射された反射光１ｅとが干渉し、この干渉した反射光１ｃが検出器５に導かれる。そして次に検出器５に導かれた干渉された反射光１ｃから得られる信号を情報処理手段７で上記のように演算処理することによって、測定を目的とする所望の生体組織の性状を定量して測定することができるのである。

【００２１】上述のように従来からおこなわれている７５０～２５００ｎｍの波長の近赤外光（近赤外領域）を用いた分光分析方法は、一般的に目的とする成分に関連するシグナル（信号）が小さく、その帰属が明確でない場合が多いので定量分析が困難であるとされている。このために従来ではＳＮ比を改善するために、ある基準シグナルと目的シグナル（測定を目的とする生体組織からのシグナル）との差をとったり、その比をとって規格化するなどの前処理をし、多変量解析手法を応用することで目的の生体組織の目的の成分の定量をおこなっている。

【００２２】また従来の分光分析方法では、複数の波長を含むある光源からの光を干渉フィルタあるいは回折格子により時系列的に分光し、その分光された光を順次、比測定物に照射し、透過あるいは反射した光の強さを検知することによって、各波長帯における吸光度や透過度をそれぞれ求めている。しかしこの手法を生体組織性状の測定に適用した場合、光が透過あるいは反射する複雑な生体組織の構成成分に帰属するすべての情報が重畳したスペクトルとして検出されることになり、つまりは測定を意図（目的）とする所望の生体組織以外に由来（帰属）するシグナルも含まれたスペクトルとなる。そのために目的とする所望の生体組織の成分に帰属するシグナルに対するノイズ成分が増大してＳＮ比が低下してしまうのである。

【００２３】しかし本発明の上記生体組織性状測定装置では、生体組織で反射された反射光１ｄと反射鏡４で反射された反射光１ｅとを干渉させて検出器５に導くようにしたので、生体組織で反射された反射光１ｄのうち反射鏡４で反射された反射光１ｅと位相が一致する反射光

を強めて検出器５に導くことができ、反射鏡４で反射された反射光１ｅと位相が一致する反射光を反射する生体組織の成分に帰属するシグナルに対するノイズ成分を低減させてＳＮ比を向上させることができるのである。

【００２４】反射鏡４で反射された反射光１ｅと位相が一致する反射光を反射する生体組織と反射光１ｅ、１ｄが互いに干渉する点との間の距離は、反射鏡４と前記反射光１ｅ、１ｄが互いに干渉する点との間の距離と一致するものであり、従って反射鏡４と前記反射光１ｅ及び反射光１ｄが干渉する点との間の距離を求めることによって生体３のどの位置の生体組織から反射された反射光が干渉によって強められているかを検知することができる。

【００２５】また上記反射鏡４は生体組織で反射された反射光１ｄに対して移動自在に形成したので、反射光１ｅ及び反射光１ｄが干渉する点と反射鏡４の位置を自由に設定することができるものである。従って反射鏡４を上記反射光１ｅ及び反射光１ｄが干渉する点に対して移動させることによって、生体３の深さ方向における任意の位置に存在する生体組織からの反射光の位相と反射鏡４で反射される反射光１ｅの位相とを一致させることができ、測定の対象となる所望の生体組織からの反射光を選択的に強めることができるものであり、このために測定の対象となる所望の生体組織の成分に帰属するシグナルに対するノイズ成分を低減させてＳＮ比を向上させることができるのである。

【００２６】本発明の生体組織性状測定装置は、生体組織細胞中あるいは生体組織細胞外の体液成分の濃度の定量を一つの目的とするものである。この体液成分の濃度の定量には、水の第一倍音付近の領域（１２５０～１８００ｎｍ）の近赤外光１と、水の第二倍音付近の領域（８００～１３００ｎｍ）の近赤外光１のうち、一方あるいは両方を利用することによっておこなう。各領域の特性としては、水の第一倍音付近の領域では、分子振動に帰属するスペクトル信号が大きい反面、光の透過性が悪く、水の第二倍音付近の領域では、分子振動に帰属するスペクトル信号が小さい反面、光の透過性に富むのである。

【００２７】また上記体液成分の濃度の定量がグルコース濃度の定量である場合には、光源９から照射される近赤外光１としては、９５０～１１５０ｎｍ及び１２５０～１８００ｎｍの波長領域から選択した全領域あるいは領域の一部からなる少なくとも一種類の波長のコヒーレント近赤外光、特に、９４５±２０ｎｍ、９６５±２０ｎｍ、１０１５±３０ｎｍ、１１００±３０ｎｍ、１４００±２０ｎｍ、１４５０±２０ｎｍ、１５００±２０ｎｍ、１６８０±２０ｎｍの波長のコヒーレント近赤外光を用いる必要がある。

【００２８】つまりグルコース濃度の定量には、水の第一倍音付近の領域の信号として９５０～１１５０ｎｍ、好ましくは９４５±２０ｎｍ、９６５±２０ｎｍ、１０１５±３０ｎｍ、１１００±３０ｎｍを、水の第二倍音付近の領域の信号として１２５０～１８００ｎｍ、好ましくは１４００±２０ｎｍ、１４５０±２０ｎｍ、１５００±２０ｎｍ、１６８０±２０ｎｍのシグナルの少なくとも一波長を用いて測定する必要がある。

【００２９】このようにグルコース濃度の定量に９５０～１１５０ｎｍ、好ましくは９４５±２０ｎｍ、９６５±２０ｎｍ、１０１５±３０ｎｍ、１１００±３０ｎｍを、１２５０～１８００ｎｍ、好ましくは１４００±２０ｎｍ、１４５０±２０ｎｍ、１５００±２０ｎｍ、１６８０±２０ｎｍのシグナル（近赤外光１）の少なくとも一波長を用いて測定することによって、グルコース濃度を精度よく定量分析することができるものである。

【００３０】測定された各波長の信号は、前もって作成された検量線（検量式）を用いて情報処理手段７でグルコース濃度に変換されて、表示装置８で測定値として表示される。検量線（検量式）の作成は通常数種類の波長を用いて作成されるが、本発明においては前記波長を含むものであれば、測定波長や数のいずれも制限するものではない。

【００３１】また血糖値の代用特性として生体組織細胞中あるいは生体組織細胞外のグルコース濃度を定量するには、皮下０．１～１０．０ｍｍの間、好ましくは０．５～１０．０ｍｍの間の位置にある目的とする（測定の対象の）生体組織からの反射光（散乱光）１ｄに干渉させるように反射鏡４の位置を設定することができ、このことで、血糖値の代用特性としてのグルコース濃度を精度よく定量分析することができるものである。

【００３２】また生体組織細胞中あるいは生体組織細胞外の体液成分の濃度の定量、特にグルコース濃度を定量をおこなうにあたっては、生体３の体表面近傍を流れる動脈あるいは静脈からの反射光１ｄに反射鏡４からの反射光１ｅを干渉させて測定するの非常に良い方法である。その際血管を流れる血液は散乱が大きい特性があって測定に利用しにくいので、近赤外光１のビームスプリッタ２で分割された他方の光１ｂが照射される側の血管近傍、つまり血管の体表面側近傍の生体組織での反射光が反射鏡４からの反射光１ｅと干渉するように反射鏡４の位置を調整して設定すると、良いスペクトル（信号）が得られる。

【００３３】またＳＮ比の良い（高い）スペクトルを得るという観点から、グルコース濃度の定量には皮下脂肪組織を避けて測定をおこなう必要がある。そのために、反射鏡４の位置を移動させて測定における適切な設定位置を見つけることは非常に有効であり、その脂肪組織の位置を検出するにあたっては、グルコース濃度の定量に好ましくない脂肪組織の特徴的な光の吸収を用いておこなう。この脂肪組織での光の吸収の大小の測定をおこなうにあたっては、少なくとも９００～９５０ｎｍあるい

は１３５０～１４２０ｎｍの波長領域の全領域あるいは領域の一部からなるコヒーレント近赤外光１を用いておこない、この吸収が脂肪組織によるものか否かを比較して判断する。

【００３４】本発明の生体組織性状測定装置のもう一つの目的は、生体組織性状が生体組織の固さや密度のような物性であって、この物性を定性分析あるいは定量分析することにある。生体組織の固さや密度のような物性とは、具体的には肩こりに代表される身体のこり、あるいは乳癌や肝硬変や脂肪肝や動脈硬化に代表される生体組織の変化である。

【００３５】このような生体組織性状の分析には、多数の被験者から得られるスペクトルを定量分析あるいは定性分析を利用しておこなわれる。定量分析には線形重回帰分析（ＭＬＲ）、主成分回帰分析、ＰＬＳ回帰分析（partial least squares regressin ）、ニューラルネット手法、ニューラルネット手法が用いられ、定性分析には判別分析、クラスタ分析等の手法が利用することができる。

【００３６】生体組織の固さや密度のような物性を分析（測定）する生体組織性状測定装置も上記と同様に形成することができる。分析に利用する光源９から照射される近赤外光１の波長や情報処理手段７における検量手法の決定は、多数の正常組織と病変組織のスペクトル（信号）を解析することによりおこなうが、分析に利用する光源９から照射される近赤外光１の波長や情報処理手段７における検量手法の他の決定手法としては、予め動物実験等により侵襲的におこなう方法がある。この方法は侵襲的に露出させた被測定組織（正常組織及び病変組織の両方）に回折格子やＦＴ－ＩＲ等の手法により分光した光を照射して吸収スペクトルを得て、この吸収スペクトルを多変量解析することにより、本発明の生体組織性状測定装置に利用する近赤外光１の波長や情報処理手段７における検量手法を決定し、この決定した近赤外光１の波長や情報処理手段７における検量手法を利用して上述のように本発明の生体組織性状測定装置による生体組織性状の測定（in vivo 測定）をおこなうようにする。

【００３７】具体例を挙げると、人為的に癌化させたマウスの癌組織を表皮組織を切開することにより露出させ、上記手法で癌組織のスペクトルを得る。また同様の操作を正常なマウスを含む多数のマウスに実施してスペクトルを得、次にこれらスペクトルを定性分析することにより、組織性状の判別に意味のある波長をピックアップして、本発明の生体組織性状測定装置に利用する近赤外光１の波長を決定する。そしてこの決定した波長の近赤外光１を本発明の生体組織性状測定装置による生体組織の性状の分析をおこなうことによって、生体組織で癌発症を判別することができる。

【００３８】尚、本発明の生体組織性状測定装置の分析精度を上げるには、さらに本発明の生体組織性状測定装置による分析を非侵襲的に多数の生体組織に施して、多変量解析する必要がある。また上にも述べたが、本発明の生体組織性状測定装置を用いて侵襲的な実験を経ずに非侵襲的な段階から分析を実施しても、生体組織の固さや密度のような物性を分析することは可能である。

【００３９】次に本発明の生体組織性状測定装置の実施例を説明する。図１に示す生体組織性状測定装置は、生体組織性状として生体組織中のグルコース濃度を測定するものである。光源９として１６７０ｎｍと１４５０ｎｍの波長のコヒーレント近赤外光１を照射するコヒーレントレーザ光源を用いている。６は光源９から照射されたコヒーレント近赤外光１を集光する凸型のレンズである。光源９から照射されたコヒーレント近赤外光１を二つに分割するビームスプリッタ２は、レンズ６と被測定物である生体（腕）３の間に配置されており、レンズ６を介して照射されるコヒーレント近赤外光１の進行方向に対して約４５° 傾けられている。レンズ６を介してビームスプリッタ２に照射されたコヒーレント近赤外光１は、このコヒーレント近赤外光１の進行方向に対して約９０° に進行する光１ａと、コヒーレント近赤外光１の進行方向と略平行な方向に進行する光１ｂとに分割され、上記光１ａはコヒーレント近赤外光１の進行方向と略平行に配置される反射鏡４に導かれると共に上記光１ｂは生体３に導かれる。図１に矢印で示すように反射鏡４は上記スプリッタ２に対して近接離隔するように移動自在に形成されている。

【００４０】上記光１ａは反射鏡４でビームスプリッタ２の方に反射光１ｅとして反射されると共に上記光１ｂは生体３中の任意の位置の生体組織でビームスプリッタ２の方に反射光１ｄとして反射され、両方の反射光１ｅ、１ｄはビームスプリッタ２の位置で互いに干渉するが、皮下２ｍｍに位置する生体組織からの反射光の位相と反射鏡４からの反射光１ｅの位相とが一致するように（干渉するように）、ビームスプリッタ２（反射光１ｄ、１ｅの干渉の位置）からの反射鏡４の位置を設定してある。このように皮下２ｍｍに位置する生体組織からの反射光の位相と反射鏡４からの反射光１ｅの位相とが一致するようにビームスプリッタ２の干渉の位置からの反射鏡４の位置を設定することによって、皮下２ｍｍに位置する生体組織からの反射光を選択的に強めることができる。

【００４１】この干渉した反射光１ｃは反射板４と略正面に対向する凸型のレンズ１０で集光されて検出器（受光素子）５に導かれる。この後検出器５で電圧に変換された反射光１ｃからの信号をデジタル化してマイクロコンピュータである情報処理手段７に入力し、上記信号を予め用意された検量線に従って情報処理手段７で演算処理することによってグルコース濃度が算出され、このグルコース濃度が測定値として表示手段８に表示されるようになっている。

【００４２】グルコース濃度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られるグルコース濃度の真値と、本発明によるコヒーレント近赤外光１の吸光度の関係を統計的解析手段により解析することで得ることができる。また上記他の標準手法での生体組織のグルコース濃度の定量が困難な場合は、代用特性として血液中のグルコース濃度（血糖値）を用いて検量線を作成してもよい。この場合、本発明を逆に血糖値測定装置として利用することができる。

【００４３】また本発明の利用者本人より検量線を作成する場合にあたっては、グルコース負荷試験を用いることができる。これは先ずグルコース含有物を飲料後、一定時間間隔で採血と上記本発明による信号測定をおこなうようにする。次に採血した血液を分析する標準手法により得られたグルコース濃度と、本発明の測定時に記憶された信号とを対比してデータ化し、このデータを用いて情報処理手段７に内蔵される解析手段により検量線が作成される。この実施例において個人対応の検量線を作成する場合には重回帰分析手法を用いている。

【００４４】次に他の実施例を説明する。この実施例のものは生体組織性状として生体組織中のグルコース濃度を測定するものである。光源９としてはタングステンハロゲンランプと回折格子からなる光源を用いており、この回折格子を用いることによって９５０～１１５０ｎｍの波長領域のスペクトルを測定してグルコースの定量をおこなうようにしている。また皮下２ｍｍに位置する生体組織からの反射光の位相と反射鏡４からの反射光１ｅの位相とが一致するように（干渉するように）反射鏡４の位置が設定されている。これら以外は上記実施例と同様に図１に示すように形成されている。

【００４５】またグルコース濃度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られるグルコース濃度の真値と、本発明によるコヒーレント近赤外光１の吸光度の関係を統計的解析手段により解析することで得た。またこの実施例において個人対応の検量線を作成する場合にはＰＬＳ回帰分析手法を用いている。

【００４６】次にさらに他の実施例を説明する。この実施例のものは生体組織性状として生体組織中のグルコース濃度を測定するものである。光源９としてはタングステンハロゲンランプと回折格子からなる光源を用いており、この回折格子を用いることによって１２５０～１８００ｎｍの波長領域のスペクトルを測定してグルコースの定量をおこなうようにしている。また皮下２ｍｍに位置する生体組織からの反射光の位相と反射鏡４からの反射光１ｅの位相とが一致するように（干渉するように）反射鏡４の位置が設定されている。これら以外は上記実施例と同様に図１に示すように形成されている。

【００４７】またグルコース濃度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られるグルコース濃度の真値と、本発明によるコヒーレント近赤外光１の吸光度の関係を統計的解析手段により解析することで得た。またこの実施例において個人対応の検量線を作成する場合にはＰＬＳ回帰分析手法を用いている。

【００４８】次にさらに他の実施例を説明する。この実施例のものは生体組織性状として生体組織中のグルコース濃度を測定するものである。光源９としてはタングステンハロゲンランプと干渉フィルタからなる光源を用いており、使用した干渉フィルタは中心波長が１４００ｎｍ、１５００ｎｍ、１６８０ｎｍで半値幅が２０ｎｍのものであった。また皮下２ｍｍに位置する生体組織からの反射光の位相と反射鏡４からの反射光１ｅの位相とが一致するように（干渉するように）反射鏡４の位置が設定されている。これら以外は上記実施例と同様に図１に示すように形成されている。

【００４９】またグルコース濃度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られるグルコース濃度の真値と、本発明によるコヒーレント近赤外光１の吸光度の関係を統計的解析手段により解析することで得た。またこの実施例において個人対応の検量線を作成する場合には重回帰分析手法を用いている。

【００５０】次にさらに他の実施例を説明する。この実施例のものは生体組織性状として生体組織中のグルコース濃度を測定するものである。光源９としてはタングステンハロゲンランプと干渉フィルタからなる光源を用いており、使用した干渉フィルタは中心波長が９４５ｎｍ、９６５ｎｍ、１０１５ｎｍ、１１００ｎｍで半値幅が２０ｎｍのものであった。また皮下２ｍｍに位置する生体組織からの反射光の位相と反射鏡４からの反射光１ｅの位相とが一致するように（干渉するように）反射鏡４の位置が設定されている。これら以外は上記実施例と同様に図１に示すように形成されている。

【００５１】またグルコース濃度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られるグルコース濃度の真値と、本発明によるコヒーレント近赤外光１の吸光度の関係を統計的解析手段により解析することで得た。またこの実施例において個人対応の検量線を作成する場合には重回帰分析手法を用いている。

【００５２】次にさらに他の実施例を説明する。この実施例のものは生体組織性状として生体組織中のグルコース濃度を測定するものである。光源９としてはタングステンハロゲンランプと回折格子からなる光源を用いており、この回折格子を用いることによって１２５０～１８００ｎｍの波長領域のスペクトルを測定することにより

グルコース濃度の定量をおこなっている。またこの実施例では、近赤外光１から分割された光１ｂを生体（腕）３の皮静脈に向けて照射し、静脈血の反射スペトルを測定するようにしている。反射鏡４の位置は上記皮静脈血管の体表面側の面からの反射光の位相と反射鏡４からの反射光１ｅの位相とが一致するように（干渉するように）調節して設定されている。このような反射鏡４の位置は、血液の散乱が大きいことを利用して反射鏡４の位置を調節して、皮静脈血管の体表面側の面からの反射光において大きなゲイン（利得）が得られるところで固定するようにしている。これら以外は上記実施例と同様に図１に示すように形成されている。

【００５３】またグルコース濃度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られるグルコース濃度の真値と、本発明によるコヒーレント近赤外光１の吸光度の関係を統計的解析手段により解析することで得た。またこの実施例において個人対応の検量線を作成する場合にはＰＬＳ回帰分析手法を用いている。

【００５４】次にさらに他の実施例を説明する。この実施例のものは生体組織性状として生体組織中のグルコース濃度を測定するものである。光源９としてはタングステンハロゲンランプと回折格子からなる光源を用いており、この回折格子を用いることによって９５０～１１５０ｎｍの波長領域のスペクトルを測定することによりグルコース濃度の定量をおこなっている。またこの実施例ではグルコース濃度の測定に先立ち、９００～９５０ｎｍの近赤外光１を用いて上記と同様のスペクトルの測定をおこない、これにより脂肪組織での反射光１ｄであるか否かを判定し、脂肪組織でのスペクトルでないことを確認している。この判定には定性分析手法を利用した。これら以外は上記実施例と同様に図１に示すように形成されている。

【００５５】またグルコース濃度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られるグルコース濃度の真値と、本発明によるコヒーレント近赤外光１の吸光度の関係を統計的解析手段により解析することで得た。またこの実施例において個人対応の検量線を作成する場合にはＰＬＳ回帰分析手法を用いている。

【００５６】次にさらに他の実施例を図２に基づいて説明する。この実施例のものは生体（肩）３の生体組織性状として肩こりを測定するものである。光源９としてはタングステンハロゲンランプと回折格子からなる光源を用いており、この回折格子を用いることによって９５０～１１５０ｎｍの波長領域のスペクトルを測定することにより生体組織の固さの定性分析をおこなっている。またこの実施例ではビームプリット２で分割された光１ｂを肩部分に照射し、これで得られるスペクトルを上記と同様に分析して定性分析を実施している。これら以外は上記実施例と同様に図１に示すように形成されている。

【００５７】また肩こりの程度を算出するために使用する検量線は、本発明の利用者あるいは複数の人間を被験者とし、本発明とは異なる他の標準手法により得られる肩こりの程度と、本発明によるコヒーレント近赤外光１の吸光度の関係を統計的解析手段により解析することで得た。肩こりの程度はプロのマッサージ師による触診から得られる５段階評価の値を用いた。またこの実施例において個人対応の検量線を作成する場合にはＰＬＳ回帰分析手法を用いている。

【００５８】

【発明の効果】上記のように本発明の請求項１に記載の発明は、コヒーレントあるいはそれに近い近赤外光を二つに分割するビームスプリッタと、分割された近赤外光のうち一方の光を生体組織で反射される他方の光と干渉させるように反射する反射鏡と、干渉させた反射光の信号を検出する検出器と、検出器で検出された信号を演算処理する情報処理手段とを備え、生体組織で反射された反射光に対する反射鏡の位置を設定自在に形成したので、分割された近赤外光のうち一方の光を生体組織で反射される他方の光と干渉させるように反射鏡で反射することによって、反射鏡で反射された反射光の位相と一致する位相の生体組織で反射された反射光を選択的に強めることができ、反射鏡で反射された反射光の位相と一致する位相の反射光を反射する生体組織の性状分析を非侵襲で精度良く分析することができる、つまり生体組織の成分や組織の濃度変化や物性変化に関連する信号をより明確にして正確な生体組織性状の定量分析あるいは定性分析をおこなうことができるものである。

【００５９】しかも生体組織で反射された反射光に対する反射鏡の位置を設定自在に形成することによって、生体の任意の位置の生体組織からの反射光の位相と反射鏡で反射された反射光の位相とを一致させることができ、生体の任意の位置の分析を目的とする組織あるいは組織近傍からの反射光を選択的に検知することができるものである。

【００６０】また本発明の請求項２に記載の発明は、前記生体組織性状が生体組織の細胞中あるいは生体組織の細胞外の体液成分濃度であるので、生体組織の細胞中あるいは生体組織の細胞外の体液成分濃度を非侵襲で精度良く分析することができるものである。また本発明の請求項３に記載の発明は、前記生体組織性状である体液成分濃度がグルコース濃度であって、前記グルコース濃度の定量にあたって少なくとも９５０～１１５０ｎｍ及び１２５０～１８００ｎｍの領域から選択された全領域あるいは領域の一部からなる少なくとも一種類の波長のコヒーレント近赤外光を用いたので、グルコース濃度を非侵襲で精度良く分析することができるものである。

【００６１】また本発明の請求項４に記載の発明は、皮下０．１～１０．０mmの間の生体組織で反射された反射光に反射鏡で反射された反射光を干渉させるように前記反射鏡の位置を設定したので、血糖値の代用特性として生体組織のグルコース濃度を測定するにあたって、グルコース濃度を非侵襲で精度良く分析することができるものである。

【００６２】また本発明の請求項５に記載の発明は、前記生体組織が体表面近傍の動脈血管あるいは静脈血管の体表側近傍であって、この生体組織で反射された反射光に反射鏡で反射された反射光を干渉させるように前記反射鏡の位置を設定したので、散乱の小さい体表面近傍の動脈血管あるいは静脈血管の体表側近傍からの反射光の位相と反射鏡で反射された反射光の位相を一致させることによって、散乱の大きい血液からの反射光の位相と反射鏡で反射された反射光の位相を一致させる場合よりも、生体性状、特にグルコース濃度を非侵襲で精度良く分析することができるものである。

【００６３】また本発明の請求項６に記載の発明は、所望の生体組織の組織性状を測定するのに好ましくない組織成分の光の吸収の大小の測定に基づいて、前記反射鏡の位置を設定したので、所望の生体組織の組織性状を測定するのに好ましくない組織成分からの反射光の位相と反射鏡で反射された反射光の位相を一致させないようにすることができ、生体性状を非侵襲で精度良く分析することができるものである。

【００６４】また本発明の請求項７に記載の発明は、前記好ましくない組織成分が脂肪組織であって、９００～９５０nm及び１３５０～１４２０nmの少なくとも一方の波長領域の全領域あるいは領域の一部からなるコヒーレント近赤外光を用いると共に反射鏡を移動させることによって脂肪組織での上記コヒーレント近赤外光の吸収の大小を検出したので、脂肪組織からの反射光であるか否かを精度良く分析することができるものである。

【００６５】また本発明の請求項８に記載の発明は、前記生体組織性状が生体組織の固さや密度等の物性であるので、生体組織の性状のうち上記物性の分析を非侵襲で精度良く分析することができるものである。

【図面の簡単な説明】

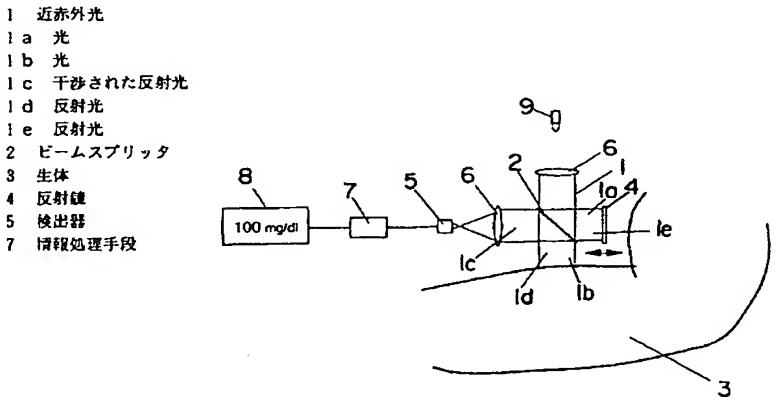
【図１】本発明の一実施の形態を示す概略図である。

【図２】同上の他の実施の形態を示す概略図である。

【符号の説明】

１　近赤外光
１ａ　光
１ｂ　光
１ｃ　干渉された反射光
１ｄ　反射光
１ｅ　反射光
２　ビームスプリッタ
３　生体
４　反射鏡
５　検出器
７　情報処理手段

【図１】



【図２】